PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
AY/gs/2004.1234		
International application No.	International filing date (*day/month/year*)	Priority Date (*day/month/year*)
PCT/SG 2004/000094	15 April 2004 (15.04.2004)	18 July 2003 (18.07.2003)

International Patent Classification (IPC) or national classification and IPC

IPC[7]: C08F 290/00, C08F 2/22, C08F 2/50, A61K 31/74, A61K 9/50, A61L 15/22, C12N 5/00

Applicant

AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH

1. This international preliminary examination report has been prepared by this International Preliminary Examination Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

- I. ☒ Basis of the opinion
- II. ☐ Priority
- III. ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV. ☐ Lack of unity of invention
- V. ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI. ☐ Certain documents cited
- VII. ☐ Certain defects in the international application
- VIII. ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18.02.2005	3 October 2005 (03.10.2005)
Name and mailing address of the IPEA/AT Austrian Patent Office Dresdner Straße 87 A-1200 Vienna Facsimile No. 1/53424/200	Authorized officer PUSTERER F. Telephone No. 1/53424/311

Form PCT/IPEA/409 (cover sheet) (July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/SG 2004/000094

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:
pages 1-26, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:
pages _____, as originally filed
pages _____, as amended (together with any statement) under Article 19
pages _____, filed with the demand
pages 27-32, filed with the letter of 18 February 2005 (18.02.2005).

☒ the drawings:
pages 1-7, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as „originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/SG 2004/000094

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☐ claims Nos. .

because:

☒ the said international application, or the said claims Nos. 21-25 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

Although claims 21 to 25 are directed to a method of treatment of the human or animal body by therapy (see Rule 39.1 iv PCT) the preliminary examination has been carried out and based on the alleged effects of the claimed thermosensitive nanoporous polymer.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/SG 2004/000094

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-45	YES
	Claims	----	NO
Inventive step (IS)	Claims	1-45	YES
	Claims	----	NO
Industrial applicability (IA)	Claims	1-45	YES
	Claims	----	NO

Citations and explanations (Rule 70.7)

The following documents have been cited in the Search Report:

D1: US 5399618 A
D2: US 5296627 A
D3: EP 217485 A2
D4: US 5721313 A
D5: US 5294692 A
D6: US 4806609 A
D7: US 5874495 A
D8: WO 1997/005185 A2
D9: US 5410016 A
D10: US 2002/0187182 A1
D11: US 2002/0120015 A1
D12: US 5587143 A

The amendments filed with the letter dated 18 February 2005 (18.05.2005) do not go beyond the content of the application as originally filed.

In the light of the comments the subject-matter of the new claims 1-45 filed with this letter can be considered inventive and inventive.

Additionally the subject-matter of the new claims 1 to 45 can be industrially applied undoubtedly.

Therefore, the present application meets the criteria as defined in the regulations (Article 33 (2) – (4) PCT).

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The term "fluronic68-diacrylate" used in claim 5 and the terms "fluronic68-diacrylate" and "fluronic 68" on pages 8 and18, paragraphs [0038], [0086] and [0087], appear to concern a registered trade mark (pluronic) and should be identified as such - rule10.1(d) PCT: "...for chemical formulae, the symbols, atomic weights, and molecular formulae, in general use, shall be employed."

Product claims 29 & 30 are not clear, because a polymer/membrane cannot be characterized by the matter of preparing the same.

With regard to claims 1 to 20 and particularly claim 29, the subject-matter of claim 31 doesn't need any protection requirement.
Therefore, claim 31 should be deleted.

WHAT IS CLAIMED IS:

1. A process for preparing a thermosensitive nanoporous polymer comprising polymerizing a microemulsion comprising a first monomer that is capable of forming a thermosensitive polymer and a polymerizable surfactant.

2. The process of claim 1 wherein the first monomer is an acrylamide derivative.

3. The process of claim 2 wherein the first monomer is an alkylated acrylamide.

4. The process of claim 3 wherein the first monomer is *N*-isopropylacrylamide.

5. The process of claim 4 wherein the polymerizable surfactant is ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate or fluronic68-diacrylate.

6. The process of claim 5 wherein the microemuision comprises a comonomer.

7. The process of claim 6 wherein the microemulsion comprises methyl methacrylate or 2-hydroxyethyl methacrylate.

8. The process of claim 7, wherein the polymerizable surfactant is ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate and the microemulsion further comprises a chemical cross-linker.

9. The process of claim 8, wherein the cross-linker is EGDMA.

10. The process of claim 9, wherein the microemulsion further comprises a photo-initiator.

11. The process of claim 10, wherein the photo-initiator is 2,2-dimethoxy-2-phenylacetophenone.

12. The process of claim 11, wherein the polymerizing comprises subjecting the microemulsion to ultraviolet radiation.

13. The process of claim 12 comprising the step of preparing a layer of microemulsion of a desired thickness prior to polymerization.

14. The process of claim 13, wherein the microemulsion comprises about 20 % (w/w) *N*-isopropylacrylamide, about 10% (w/w) methyl methacrylate, about 10 % (w/w) 2-hydroxyethyl methacrylate, about 35 % (w/w) ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, about 23% (w/w) water and about 2% ethylene glycol dimethacrylate.

15. The process of claim 13, wherein the microemulsion comprises about 10 % (w/w) *N*-isopropylacrylamide, about 10% (w/w) methyl methacrylate, about 20 % (w/w) 2-hydroxyethyl methacrylate, about 35 % (w/w) ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, about 23% (w/w) water and about 2% ethylene glycol dimethacrylate.

16. The process of claim 13, wherein the microemulsion comprises about 7.5 % (w/w) *N*-isopropylacrylamide, about 7.5 % (w/w) methyl methacrylate, about 15 % (w/w) 2-hydroxyethyl methacrylate, about 35 % (w/w) ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, about 33% (w/w) water and about 2% ethylene glycol dimethacrylate.

17. The process of claim 13, wherein the microemulsion comprises about 10 % (w/w) *N*-isopropylacrylamide, about 20 % (w/w) methyl methacrylate, about 10 % (w/w) 2-hydroxyethyl methacrylate, about 35 % (w/w) ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, about 23% (w/w) water and about 2% ethylene glycol dimethacrylate.

18. The process of claim 13, wherein the microemulsion comprises about 25 % (w/w) *N*-isopropylacrylamide, about 10 % (w/w) methyl methacrylate, about 5 % (w/w) 2-hydroxyethyl methacrylate, about 35 % (w/w) ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, about 23% (w/w) water and about 2% ethylene glycol dimethacrylate.

19. The process of claim 13, wherein the microemulsion comprises about 30 % (w/w) *N*-isopropylacrylamide, about 10 % (w/w) 2-hydroxyethyl methacrylate, about 35 % (w/w) ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, about 23% (w/w)

water and about 2% ethylene glycol dimethacrylate.

20. The process of claim 13, wherein the microemulsion comprises about 10 % (w/w) *N*-isopropylacrylamide, about 25 % (w/w) methyl methacrylate, about 5 % (w/w) 2-hydroxyethyl methacrylate, about 35 % (w/w) ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, about 23% (w/w) water and about 2% ethylene glycol dimethacrylate.

21. A method of dressing and undressing a wound comprising:

applying a thermosensitive nanoporous polymer to a wound;

immediately prior to removing the polymer from the wound, reducing the temperature of thermosensitive nanoporous polymer to facilitate removal of the polymer; and

removing the thermosensitive nanoporous polymer from the wound.

22. A method of delivering a therapeutic agent to a wound comprising:

incorporating a therapeutic agent into a thermosensitive nanoporous polymer; and

applying the thermosensitive nanoporous polymer to the wound.

23. The method of claim 22, wherein the therapeutic agent is a drug, an antibiotic, an anti-inflammatory agent, a clotting factor, a hormone, a nucleic acid, a peptide, a cellular factor, or a ligand for a cell surface receptor.

24. The method of claim 22, wherein the therapeutic agent is a drug or an antibiotic.

25. The method of claim 22, wherein the therapeutic agent is a wound healing accelerator.

26. A method of delivering a cell to a graft site comprising:

culturing the cell on a thermosensitive nanoporous polymer; and

placing the polymer comprising the cell onto the graft site.

27. The method of claim 26, further comprising:

reducing the temperature of the thermosensitive nanoporous polymer to facilitate removal of the polymer; and

removing the polymer from the graft site.

28. The method of claim 27, wherein the step of reducing the temperature is performed after placing the thermosensitive nanoporous polymer carrying the cell onto the graft site.

29. A thermosensitive nanoporous polymer when prepared by the process of any one of claims 1 to 20.

30. A thermosensitive nanoporous membrane when prepared by the process of claim 13.

31. A thermosensitive polymer which is nanoporous.

32. The thermosensitive nanoporous polymer of claim 31 having a decomposition temperature of at least about 300°C.

33. The thermosensitive nanoporous polymer of claim 32 having a water vapour transmission rate of about 500 to about 2000 $g/m^2/day$.

34. The thermosensitive nanoporous polymer of claim 33 having a tensile strength of about 4 to about 20 MPa.

35. The thermosensitive polymer of claim 34 formed from a microemulsion comprising a first monomer capable of forming a thermosensitive polymer and a polymerizable surfactant.

36. The thermosensitive nanoporous polymer of claim 35 wherein the first monomer

is *N*-isopropylacrylamide.

37. The thermosensitive nanoporous polymer of claim 36 wherein the polymerizable surfactant is ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate or fluronic68-diacrylate.

38. The thermosensitive nanoporous polymer of claim 37, wherein the microemulsion comprises *N*-isopropylacrylamide, methyl methacrylate, 2-hydroxyethyl methacrylate, ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, water and ethylene glycol dimethacrylate in a ratio of approximately 20:10:10:35:23:2.

39. The thermosensitive nanoporous polymer of claim 37, wherein the microemulsion comprises *N*-isopropylacrylamide, methyl methacrylate, 2-hydroxyethyl methacrylate, ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, water and ethylene glycol dimethacrylate in a ratio of approximately 10:10:20:35:23:2.

40. The thermosensitive nanoporous polymer of claim 37, wherein the microemulsion comprises *N*-isopropylacrylamide, methyl methacrylate, 2-hydroxyethyl methacrylate, ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, water and ethylene glycol dimethacrylate in a ratio of approximately 7.5:7.5:15:35:33:2.

41. The thermosensitive nanoporous polymer of claim 37, wherein the microemulsion comprises *N*-isopropylacrylamide, methyl methacrylate, 2-hydroxyethyl methacrylate, ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, water and ethylene glycol dimethacrylate in a ratio of approximately 10:20:10:35:23:2.

42. The thermosensitive nanoporous polymer of claim 37, wherein the microemulsion comprises *N*-isopropylacrylamide, methyl methacrylate, 2-hydroxyethyl methacrylate, ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, water and ethylene glycol dimethacrylate in a ratio of approximately 25:10:5:35:23:2.

43. The thermosensitive nanoporous polymer of claim 37, wherein the microemulsion

comprises *N*-isopropylacrylamide, 2-hydroxyethyl methacrylate, ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, water and ethylene glycol dimethacrylate in a ratio of approximately 30:10:35:23:2.

44. The thermosensitive nanoporous polymer of claim 37, wherein the microemulsion comprises *N*-isopropylacrylamide, methyl methacrylate, 2-hydroxyethyl methacrylate, ω-methoxy poly(ethylene oxide)$_{40}$ undecyl α-methacrylate, water and ethylene glycol dimethacrylate in a ratio of approximately 10:25:5:35:23:2.

45. The method of claim 28 wherein the graft site is a round window membrane of an ear, or a cornea, of a subject.